TSCA HEALTH & SAFETY STUDY COVER SHEET - revised 6/25/96

TSCA CBI STATUS:

☐ **CHECK IF THIS PAGE CONTAINS CONFIDENTIAL BUSINESS INFORMATION (CBI)**

Clearly mark the confidential information with bracketing and check the box in the appropriate section (☐ *Contains CBI*). Submit a sanitized cover sheet with CBI deleted. Mark the sanitized copy, "Public Display Copy" in the heading.

1.0 SUBMISSION TYPE ☐ *Contains CBI*

Submission date: September 29, 1997

☐ 8(d) X 8(e) ☐ FYI ☐ 4 ☐ Other: specify

8EHQ - 10997 - 14029

X Initial submission ☐ Follow-up submission ☐ Final report submission

Previous EPA Submission or Title if Update or Follow-up: Docket Number, if any: #

☐ continuation sheet attached

2.1 SUMMARY/ABSTRACT ATTACHED	2.2 SUBMITTER TRACKING NUMBER OR INTERNAL ID	2.3 FOR EPA USE ON
X Yes ☐ No	8E-97-5	

8EHQ-97-14029

3.0 CHEMICAL/TEST SUBSTANCE IDENTITY ☐ *Contains CBI*

Reported Chemical Name (specify nomenclature if other than CAS name):

CAS #: 765-30-0 Cyclopropylamine

Purity: >99%

X Single Ingredient

☐ Commercial/Technical Grade

☐ Mixture Trade Name: Common Name:

	CAS Number	*Name*	*% WEIGHT*
Other chemical(s) present in tested mixture			

Contains No CBI

☐ continuation sheet attached

4.0 REPORT/STUDY TITLE ☐ *Contains CBI*

Cyclopropylamine: Acute Oral Toxicity Study in the Rat

88980000003

☐ continuation sheet attached

5.1 STUDY/TSCATS INDEXING TERMS

[CHECK ONE]

HEALTH EFFECTS (HE): X ENVIRONMENTAL EFFECTS (EE): ENVIRONMENTAL FATE (EF):

5.2 STUDY/TSCATS INDEXING TERMS (see instructions for 4-digit codes)

STUDY	SUBJECT ORGANISM	ROUTE OF	VEHICLE OF
TYPE: ATOX	(HE,EE only): RATS	EXPOSURE (HE only):GAVG	EXPOSURE (HE only): NONE
Other:	*Other:*	*Other:*	*Other:*

6.0 REPORT/STUDY INFORMATION ☐ *Contains CBI* *X Study is GLP*

Laboratory: Health and Environment Laboratories, Eastman Kodak Company Report/Study Date: September 15, 1997

1100 Ridgeway Avenue, Rochester, NY 14652

Source of Data/Study Sponsor (if different than submitter) Number of Pages: 47

☐ continuation sheet attached

7.0 SUBMITTER INFORMATION ☐ *Contains CBI*

Submitter: Marc G. Schurger Title: Director, Product Safety and Regulatory Programs Phone: (423) 229-5921

Company Name: Eastman Chemical Company Company Address: P. O. Box 1994, Kingsport TN 37664-5394

Submitter Address (if different):

Technical Contact: Karen R. Miller, Ph.D. Phone: (423) 229-1654

☐ continuation sheet attached

8.0 ADDITIONAL/OPTIONAL STUDY COMMENTS ☐ *Contains CBI*

☐ continuation sheet attached

Submitter Signature: _____ Date: _____

TSCA HEALTH & SAFETY STUDY COVER SHEET - revised 6/25/96

9.0 CONTINUATION SHEET

TSCA CBI STATUS:

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Submitter Tracking Number/Internal ID

8E 97-5

Cyclopropylamine (CPA)

This report pertains to cyclopropylamine (765-30-0). Eastman Chemical Company does not believe that the information in this report necessarily constitutes substantial risk information. It is, however, being submitted to enable the Environmental Protection Agency to make its own assessment.

The attached acute oral toxicity study shows treatment-related changes seen in rats included the following:

1) Rats which died within 48-hours of dosing : blood in the stomach and intestinal tract; edema and red discoloration of the gastric mucosa; blood in the urinary bladder; dark and enlarged spleens; wet facial hair caused by salvia; inquinal hair that was either stained by urine or discolored red by urine.

2) rats which died during the second week of the study: small thymus; adhesions of the stomach to the adjoining organs; edema and red discoloration of the gastric mucosa; a thickened non-glandular gastric mucosa; necrosis of the non-glandular gastric mucosa; small spleens; atrophy of the abdominal adipose tissue; urine-stained inguinal hair and facial hair covered with porphyrin discharge.

3) Rats which survived to termination of the observation period: adhesions of the stomach to the adjacent organs, adhesions of the liver to the diaphragm; black watery contents in the stomach and intestinal tract, necrosis of the glandular gastric mucosa, duodenum and jejunum; red discoloration, hyperkeratosis, and thickening of the gastric mucosa; atrophy of the abdominal adipose tissue; and dry porphyrin stain on the hair of the face.

The major clinical signs of abnormality observed during the 15-day observation period included body weight loss or reduced body weight gain, slight to moderate weakness, a reduced amount of feces, porphyrin staining of the hair of the face, inquinal hair wet with urine, dehydration, black diarrhea, black fecal staining of the inquinal hair, excessive salivation, blood in the urine, and either wetness or staining of the inquinal hair by urine.

The above-decribed effects were not altogether unexpected since this material was determined to be a DOT Class 8 Packing Group II Corrosive material using an *in vitro* test method (CORROSITEX™). Additionally, several aliphatic amines (isobutylamine, isopropylamine, etc.) have been reported to cause severe eye burns and severe skin irritation or burns.

If additional information concerning this study is required, please contact Karen R. Miller, Ph.D., of my staff. Her telephone number is (423) 229-1654.

C:\data\misc\CPA8(e)

FINAL REPORT

CYCLOPROPYLAMINE
SYNONYM: CPA

PM No.: 16042-00 **EAN: 108872**
HAEL No.: 97-0204 **CAS No.: 000765-30-0**

ACUTE ORAL TOXICITY STUDY IN THE RAT

GUIDELINE

OECD: 401
EEC: Annex V., Test B.1

AUTHOR

Kenneth P. Shepard, B.S.

TESTING FACILITY

Toxicological Sciences Laboratory
Health and Environment Laboratories
Eastman Kodak Company
Rochester, New York 14652-6272
USA

LABORATORY PROJECT ID

96-0204A0

STUDY SPONSOR

Eastman Chemical Company
P.O. Box 431
Kingsport, TN 37662-5280

STUDY COMPLETION DATE

September 15, 1997

QUALITY ASSURANCE INSPECTION STATEMENT
(21 CFR 58.35(B)(7), 40 CFR 792.35(B)(7), AND 40 CFR 160.35(B)(7))

STUDY: 97-0204-1 STUDY DIRECTOR: SHEPARD,K.P. PAGE 1
ACCESSION NUMBER: 108872 08/22/97

STUDY TYPE: ACUTE ORAL TOXICITY

M. L. Jones 8/25/97
(AUDITOR, QUALITY ASSURANCE UNIT) DATE

THIS STUDY WAS INSPECTED BY 1 OR MORE PERSONS OF THE QUALITY ASSURANCE UNIT. WRITTEN STATUS REPORTS WERE SUBMITTED ON THE FOLLOWING DATES.

INSPECTION DATES	PHASE(S) INSPECTED	STATUS REPORT DATES
05/20/97	PROTOCOL APPENDIX/AMENDMENT SUBMISSION	
05/22/97	CLINICAL SIGNS AT 48 HRS.	08/22/97
06/03/97	PROTOCOL AMENDMENT OF 6/3/97 RECEIVED	
07/22/97	GROSS PATHOLOGY PATHOLOGY REPORT	07/22/97
08/22/97	FINAL REPORT REVIEW	08/22/97

GOOD LABORATORY PRACTICE COMPLIANCE STATEMENT

This study was conducted according to:

Annex 2, Organisation for Economic Cooperation and Development, Guidelines for Testing of Chemicals [C(81)30(Final)].

Kenneth P. Shepard, B.S.
Study Director

September 15, 1997
Month/Day/Year

SIGNATURE PAGE

Kenneth P. Shepard, B.S.
Study Director

September 15, 1997
Month/Day/Year

Douglas C. Topping, Ph.D.
Unit Director, Mammalian Toxicology

August 31, 1997
Month/Day/Year

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ABSTRACT

CYCLOPROPYLAMINE
SYNONYM: CPA

PM No.: 16042-00 **EAN: 108872**
HAEL No.: 97-0204 **CAS No.: 000765-30-0**

ACUTE ORAL TOXICITY STUDY IN THE RAT

An acute oral toxicity study was conducted with three groups of five male and five female rats administered 250, 500, or 1000 mg/kg of the test substance by gavage. The test substance, a liquid, was administered as received. For male rats, mortality was 0% at the 250 mg/kg dose level, 20% at the 500 mg/kg dose level, and 100% at the 1000 mg/kg dose level. For female rats, mortality was 20% at the 250 mg/kg dose level, 60% at the 500 mg/kg dose level, and 80% at the 1000 mg/kg dose level. The acute oral LD_{50} for this test substance was calculated to be 616 mg/kg for male rats and 445 mg/kg for female rats.

The major clinical signs of abnormality observed during the 15-day observation period included body weight loss or a reduced body weight gain, slight to moderate weakness, a reduced amount of feces, porphyrin staining of the hair of the face, inguinal hair wet with urine, dehydration, black diarrhea, black fecal staining of the inguinal hair, excessive salivation, blood in the urine, and either wetness or staining of the inguinal hair by urine. In addition, clinical signs noted prior to death included prostration, severe weakness, convulsions, pallor, gasping, and a lack of feces.

The cause of death for rats that died after exposure to the test substance was not identified. However, the major treatment-related changes observed at necropsy provided evidence that the test substance was a gastrointestinal irritant. These changes included ptyalism; necrosis, thickening, and edema of the glandular mucosa; hyperkeratosis of the non-glandular mucosa; and necrosis of the duodenum and jejunum. Other related changes seen at necropsy included adhesions of the stomach to adjoining organs, probably caused by leakage of the gastric juices through the stomach wall, and the presence of blood in the lumen of the stomach and intestinal tract. In the absence of significant gross organ lesions other than signs of gastrointestinal irritation, no tissue was collected for microscopic examination.

Based on the oral LD_{50} calculated by combining the male and female mortality data (545 mg/kg), the test substance was classified as slightly toxic in rats according to the criteria set forth by Hodge and Sterner (1949) and harmful if swallowed as defined in the 18th Adaptation of the EC Classification, Packaging, and Labelling of Dangerous Substances Directive.

STUDY AND TEST SUBSTANCE INFORMATION

Testing Facility

Toxicological Sciences Laboratory
Health and Environment Laboratories
Eastman Kodak Company
Rochester, New York 14652-6272
USA

Project Participants

Study Director	Kenneth P. Shepard, B.S.
Principal Investigator	John W. Mosher, B.S.
Pathologist/Veterinarian	Milan S. Vlaovic, D.V.M., Ph.D.

Sponsor

Eastman Chemical Company
P.O. Box 431
Kingsport, TN 37662-5280

Sponsor's Representative:
Karen R. Miller, Ph.D.

Test Substance Characterization

Test Substance Name:	Cyclopropylamine
CAS No.:	000765-30-0
Synonyms:	CPA
HAEL No.:	97-0204
EAN:	108872
PM No.:	16042-00
SRID or Lot No.:	X25192-033
Physical State and Appearance:	Liquid, Clear, colorless
Source of Test Substance:	Eastman Chemical Company
Laboratory Project ID:	96-0204A0

Study Dates

Study Initiation Date:	May 20, 1997
Experimental Start Date:	May 20, 1997
Experimental Completion Date:	July 25, 1997

PURPOSE

The purpose of the study was to determine the estimated oral LD_{50} of the test substance in male and female rats and the clinical signs of toxicity associated with a single oral dose.

MATERIALS AND METHODS

Test system

Male and female Sprague-Dawley® rats [SAS:VAF®(SD)] obtained from SASCO, Inc., Stone Ridge (Kingston), NY were randomly assigned to each dose group. At initiation of the study, male rats were 8 weeks of age and weighed 171 to 239 grams and female rats were 8-9 weeks of age and weighed 152 to 182 grams. Rats were chosen for this study because they are a common representative species for toxicity studies. The rat is one of two primary rodent species recommended for use in the OECD Guideline.

Husbandry

Housing

Animals were housed in an American Association for Accreditation of Laboratory Animal Care-accredited vivarium in accordance with the Guide for the Care and Use of Laboratory Animals (National Research Council, 1996). The rats were singly housed in suspended, stainless-steel, wire mesh cages. Cages and racks were washed once a week. Absorbent paper, used to collect excreta, was changed at least three times a week.

Environmental Conditions

The study room was maintained at 19-23 °C and 47-59% relative humidity. A photoperiod of 12 hours light from 6 a.m. to 6 p.m. was maintained.

Acclimation Period

The animals were isolated upon arrival and allowed to acclimate for a period of 5 days. Animals were judged to be healthy prior to testing.

Husbandry, continued

Feed

Certified Rodent Diet (PMI® #5002, pelleted) was available *ad libitum*. Feed containers were cleaned weekly and refilled at least once a week. No known contaminants which would interfere with the outcome of this study were present in the feed. Analyses of feed are maintained on file within the testing laboratory.

Water

Water was available *ad libitum* through an automatic watering system. The source of the water was the local public water system. There have been no contaminants identified in periodic water analyses that would be expected to interfere with the conduct of the study. Semiannual analyses of water are maintained on file within the testing laboratory.

Identification

Upon arrival, all rats were identified by uniquely-numbered metal ear tags. During randomization, study-specific animal numbers were assigned to each animal. Cage cards contained the study-specific animal number and the ear tag number.

Experimental Design

Test Procedures

This study was conducted according to the Organisation for Economic Cooperation and Development (OECD) Guidelines for Testing of Chemicals Guideline: 401, Acute Oral Toxicity; and European Economic Community (EEC): Annex V., Test B.1 , Acute Toxicity (Oral).

Randomization

The procedure for including animals in the study was to randomly select and assign animals from the same shipment to the study. Randomization was done by computer-generated lists. After assignment of animals to the study, the body weights were determined to ensure that variation in individual body weights did not exceed 20% of the mean weight for each sex.

Experimental Design, continued

Determination of Dose Levels

Based on results of a range-finding test, doses of 250, 500, and 1000 mg/kg of the test substance were selected as the dose levels for the oral toxicity study.

Preparation of Test Substance in the Vehicle

The test substance, a liquid, was administered as received.

Test Substance Exposure

A single dose of the test substance was administered by gavage to animals that had been fasted overnight.

Distribution of Animals

TABLE 1 (Animal Distribution)

Dose Level	Number Of Animals	Animal Numbers	
		Males	Females
Range-Finding Test			
250 mg/kg	1 Male & 1 Female	251	254
500 mg/kg	1 Male & 1 Female	252	255
1000 mg/kg	1 Male & 1 Female	253	256
Oral Toxicity Study			
250 mg/kg	5 Males & 5 Females	301 - 305	316 - 320
500 mg/kg	5 Males & 5 Females	306 - 310	321 - 325
1000 mg/kg	5 Males & 5 Females	311 - 315	326 - 330

Body Weights

Body weights were collected on Days 0 (prior to treatment), 7, and 14.

Experimental Design, continued

Clinical Observations

Animals were observed three times on the day of dosing (Day 0), and once each day thereafter for the duration of the 15-day observation period. Observations included, but were not limited to, examination of the hair, skin, eyes, mucous membranes, motor activity, feces, urine, respiratory system, circulatory system, autonomic nervous system, central nervous system, and behavior patterns.

Necropsy

Any animal that died during the study was necropsied on the day of death. All surviving animals were euthanatized and necropsied at the completion of the 15-day observation period.

Data Storage

The final report, data sheets, all nonperishable raw data, and an aliquot of the test substance have been stored in the testing facility archive managed under GLP-mandated conditions.

Statistical Procedures

No statistical procedures were required during the study. No dose/mortality curve was constructed since graphs become statistically useful only with the use of large numbers of animals and dose groups.

The LD_{50} values and 95% confidence intervals were determined separately for male and female rats and, if different, for male and female rats combined according to the method of Weil (Weil, C.S., 1952).

Protocol and Standard Operating Procedure Deviations

The were no SOP or protocol deviations during the study.

RESULTS

RANGE-FINDING TEST

In a range-finding test, three male and three female rats were administered a single oral dose of 250, 500, or 1000 mg/kg. During a 14-day period, mortality included the male at the 1000 mg/kg dose level and all females at all dose levels. Based on the range-finding test, dose levels of 250, 500, and 1000 mg/kg were selected for the oral toxicity study.

ORAL TOXICITY STUDY

Mortality

For male rats, mortality was 0% at the 250 mg/kg dose level, 20% at the 500 mg/kg dose level, and 100% at the 1000 mg/kg dose level. For female rats, mortality was 20% at the 250 mg/kg dose level, 60% at the 500 mg/kg dose level, and 80% at the 1000 mg/kg dose level. The dose level, the number of animals dosed, the number of deaths, and the day of death are listed in Table 2.

TABLE 2 (Mortality Table)

Dose (mg/kg)	Number Of Rats Exposed (Male, Female)	Number Of Deaths (Male, Female)	Time Of Death
250	5,5	0,1	Day 4
500	5,5	1,3	Days 1-11
1000	5,5	5,4	Days 1-2

LD_{50} for male rats: 616 mg/kg (95% C.I. = 467 - 812)[1]
LD_{50} for female rats: 445 mg/kg (95% C.I. = 230 - 864)[1]
LD_{50} for the combined sexes: 545 mg/kg (95% C.I. = 400 - 743)[1]

[1] Calculated according to the method of Weil (Weil, C.S., 1952).

Clinical Signs

Clinical signs of abnormality observed during the 15-day observation period, the time of each observation and the number of animals involved at each dose level are listed in Table 3.

TABLE 3 (Table Of Clinical Observations)

Dose (mg/kg)	Time	Clinical Signs	Number of Animal Affected
250	Day 0	Appeared Clinically Normal	5/5 Males, 5/5 Females
250	Day 1	Appeared Clinically Normal	4/5 Males, 4/5 Females
		Slight Weakness	1/5 Females
		Stain (Porphyrin) on Hair of Face	1/5 Males, 1/5 Females
		Reduced Amount of Feces	1/5 Females
250	Day 2	Appeared Clinically Normal	1/5 Males, 4/5 Females
		Slight Weakness	3/5 Males
		Moderate Weakness	1/5 Females
		Stain (Porphyrin) on Hair of Face	1/5 Females
		Reduced Amount of Feces	4/5 Males, 1/5 Females
		Inguinal Hair Wet with Urine	1/5 Females
		Dehydration	2/5 Males, 1/5 Females
250	Day 3	Appeared Clinically Normal	5/5 Males, 4/5 Females
		Moderate Weakness	1/5 Females
		Stain (Porphyrin) on Hair of Face	1/5 Females
		Reduced Amount of Feces	1/5 Females
		Inguinal Hair Wet with Urine	1/5 Females
		Dehydration	1/5 Females
250	Day 4	Appeared Clinically Normal	3/5 Males, 4/5 Females
		Died	1/5 Females
		Slight Weakness	1/5 Males
		Stain (Porphyrin) on Hair of Face	1/5 Males
		Reduced Amount of Feces	2/5 Males
		Dehydration	1/5 Males
250	Days 5 & 6	Appeared Clinically Normal	3/5 Males, 4/4 Females
		Slight Weakness	1/5 Males
		Stain (Porphyrin) on Hair of Face	1/5 Males
		Reduced Amount of Feces	2/5 Males
		Dehydration	1/5 Males

Table continued on next page.

TABLE 3, Continued (Table Of Clinical Observations)

Dose (mg/kg)	Time	Clinical Signs	Number of Animal Affected
250	Day 7	Appeared Clinically Normal	3/5 Males, 4/4 Females
		Reduced Amount of Feces	2/5 Males
250	Days 8 to 13	Appeared Clinically Normal	5/5 Males, 4/4 Females
250	Day 14	Appeared Clinically Normal	4/5 Males, 4/4 Females
		Slight Weakness	1/5 Males
		Black Diarrhea	1/5 Males
		Stain (Black Fecal) on Inguinal Hair	1/5 Males
		Excessive Salivation	1/5 Males
		Dehydration	1/5 Males
250	Day 15	Appeared Clinically Normal	4/5 Males, 3/4 Females
		Slight Weakness	1/5 Males, 1/4 Females
		Stain (Black Fecal) on Inguinal Hair	1/5 Males
		Reduced Amount of Feces	1/4 Females
		Excessive Salivation	1/4 Females
		Dehydration	1/4 Females
500	Day 0	Appeared Clinically Normal	5/5 Males, 5/5 Females
500	Day 1	Slight Weakness	4/5 Males, 5/5 Females
		Severe Weakness (Prior to Death)	1/5 Males
		Prostration (Prior to Death)	1/5 Males
		Convulsions (Prior to Death)	1/5 Males
		Stain (Porphyrin) on Hair of Face	1/5 Males, 4/5 Females
		Reduced Amount of Feces	3/5 Males, 5/5 Females
		Inguinal Hair Wet with Urine	2/5 Males, 2/5 Females
		Discolored (Red) Urine	5/5 Males, 3/5 Females
		Stain (Red) on Inguinal Hair	1/5 Males
		Death	1/5 Males

Table continued on next page.

TABLE 3, Continued (Table Of Clinical Observations)

Dose (mg/kg)	Time	Clinical Signs	Number of Animal Affected
500	Day 2	Died	1/5 Females
		Slight Weakness	2/4 Males
		Moderate Weakness	1/4 Males, 1/4 Females
		Diarrhea	3/4 Males
		Stain (Porphyrin) on Hair of Face	1/4 Males, 2/4 Females
		Reduced Amount of Feces	4/4 Males, 4/4 Females
		Inguinal Hair Wet with Urine	1/4 Males, 2/4 Females
		Discolored (Red) Urine	1/4 Males
		Stain (Red) on Inguinal Hair	2/4 Males
		Dehydration	3/4 Males, 1/4 Females
500	Day 3	Slight Weakness	3/4 Males, 1/4 Females
		Stain (Porphyrin) on Hair of Face	2/4 Males
		Reduced Amount of Feces	4/4 Males, 4/4 Females
		Inguinal Hair Wet with Urine	1/4 Males, 1/4 Females
		Dehydration	2/4 Males, 1/4 Females
500	Day 4	Appeared Clinically Normal	1/4 Females
		Slight Weakness	3/4 Males, 1/4 Females
		Stain (Porphyrin) on Hair of Face	1/4 Males, 1/4 Females
		Reduced Amount of Feces	4/4 Males, 2/4 Females
		Inguinal Hair Wet with Urine	3/4 Males, 1/4 Females
		Dehydration	2/4 Males, 1/4 Females
500	Day 5	Appeared Clinically Normal	1/4 Males
		Slight Weakness	3/4 Males, 2/4 Females
		Stain (Porphyrin) on Hair of Face	1/4 Males, 3/4 Females
		Reduced Amount of Feces	3/4 Males, 2/4 Females
		Inguinal Hair Wet with Urine	3/4 Males, 2/4 Females
		Dehydration	2/4 Males, 2/4 Females

Table continued on next page.

TABLE 3, Continued (Table Of Clinical Observations)

Dose (mg/kg)	Time	Clinical Signs	Number of Animal Affected
500	Day 6	Appeared Clinically Normal	1/4 Males, 1/4 Females
		Slight Weakness	2/4 Males, 2/4 Females
		Stain (Porphyrin) on Hair of Face	1/4 Males, 2/4 Females
		Reduced Amount of Feces	1/4 Males, 2/4 Females
		Stain (Dried Urine) on Inguinal Hair	2/4 Males, 2/4 Females
		Dehydration	2/4 Males, 1/4 Females
500	Day 7	Appeared Clinically Normal	1/4 Males, 2/4 Females
		Slight Weakness	2/4 Males, 1/4 Females
		Moderate Weakness	1/4 Females
		Stain (Porphyrin) on Hair of Face	1/4 Females
		Reduced Amount of Feces	2/4 Females
		Stain (Dried Urine) on Inguinal Hair	2/4 Males, 2/4 Females
		Dehydration	2/4 Males, 1/4 Females
500	Day 8	Appeared Clinically Normal	1/4 Males, 2/4 Females
		Moderate Weakness	2/4 Females
		Stain (Porphyrin) on Hair of Face	1/4 Females
		Reduced Amount of Feces	2/4 Females
		Stain (Dried Urine) on Inguinal Hair	1/4 Males, 2/4 Females
		Dehydration	2/4 Males, 2/4 Females
		Excessive Salivation	1/4 Females
		Gasping (Prior to Death)	1/4 Females

Table continued on next page.

TABLE 3, Continued (Table Of Clinical Observations)

Dose (mg/kg)	Time	Clinical Signs	Number of Animal Affected
500	Day 9	Appeared Clinically Normal	3/4 Males, 2/4 Females
		Moderate Weakness	1/4 Females
		Stain (Porphyrin) on Hair of Face	1/4 Females
		Reduced Amount of Feces	1/4 Females
		Lack of Feces	1/4 Females
		Stain (Dried Urine) on Inguinal Hair	1/4 Males, 2/4 Females
		Dehydration	2/4 Females
		Hypothermia (Prior to Death)	1/4 Females
		Severe Weakness (Prior to Death)	1/4 Females
		Lack of Feces	1/4 Females
		Pallor (Prior to Death)	1/4 Females
500	Day 10	Death	1/4 Females
		Appeared Clinically Normal	4/4 Males, 2/3 Females
		Moderate Weakness	1/3 Females
		Reduced Amount of Feces	1/3 Females
		Stain (Dried Urine) on Inguinal Hair	1/3 Females
		Dehydration	1/3 Females
		Pallor (Prior to Death)	1/3 Females
500	Day 11	Death	1/3 Females
		Appeared Clinically Normal	4/4 Males, 2/2 Females
500	Days 12-13	Appeared Clinically Normal	4/4 Males, 2/2 Females
500	Day 14	Appeared Clinically Normal	3/4 Males, 1/2 Females
		Stain (Porphyrin) on Hair of Face	1/2 Females
		Inguinal Hair Wet with Urine	1/4 Males
500	Day 15	Appeared Clinically Normal	3/4 Males, 1/2 Females
		Stain (Porphyrin) on Hair of Face	1/2 Females
		Inguinal Hair Wet with Urine	1/4 Males
		Dehydration	1/4 Males

Table continued on next page.

TABLE 3, Continued (Table Of Clinical Observations)

Dose (mg/kg)	Time	Clinical Signs	Number of Animal Affected
1000	Day 0 (1 Hour)	Slight Weakness	5/5 Males, 5/5 Females
1000	Day 0 (4 Hours)	Slight Weakness Moderate Weakness Severe Weakness (Prior to Death)	2/5 Males, 1/5 Females 1/5 Males, 2/5 Females 2/5 Males, 2/5 Females
1000	Day 1	Death Moderate Weakness Severe Weakness (Prior to Death) Convulsions (Prior to Death Stain (Porphyrin) on Hair of Face Discolored (Red) Urine Reduced Amount of Feces Inguinal Hair Wet with Urine	3/5 Males, 4/5 Females 1/1 Females 2/2 Males 1/2 Males 1/2 Males, 1/1 Females 2/2 Males 2/2 Males, 1/1 Females 1/1 Females
1000	Day 2	Death Slight Weakness Stain (Porphyrin) on Hair of Face Reduced Amount of Feces Inguinal Hair Wet with Urine	2/2 Males 1/1 Females 1/1 Females 1/1 Females 1/1 Females
1000	Day 3	Slight Weakness Stain (Porphyrin) on Hair of Face Reduced Amount of Feces Inguinal Hair Wet with Urine	1/1 Females 1/1 Females 1/1 Females 1/1 Females
1000	Day 4	Slight Weakness Reduced Amount of Feces Inguinal Hair Wet with Urine	1/1 Females 1/1 Females 1/1 Females
1000	Days 5 & 6	Reduced Amount of Feces	1/1 Females
1000	Days 7 -15	Appeared Clinically Normal	1/1 Females

Urine

On the day following dosing (Day 1), discolored (red) urine was noted from a number of animals from the 500 and 1000 mg/kg dose groups. Due to this observation, all surviving animals were tested for the presence of blood in the urine using N-Multistix Reagent Strips for Urinalysis (Lot C874086/Exp 2/98) obtained from Bayer Corporation, Diagnostics Division, Elkhart, IN. Results are listed in Table 4.

TABLE 4 (Table Of Blood In The Urine)

Males			Females		
Dose (mg/kg)	Animal Number	Amount of Blood*	Dose (mg/kg)	Animal Number	Amount of Blood*
250	301	Trace-NH	250	316	Negative
250	302	Trace-NH	250	317	Large-H
250	303	Large-H	250	318	Large-H
250	304	Large-H	250	319	Moderate-NH
250	305	Large-H	250	320	Trace-NH
500	306	Large-H	500	321	Large-H
500	307	Large-H	500	322	Large-H
500	308	Large-H	500	323	Large-H
500	309	Large-H	500	324	Large-H
1000	311	Large-H	500	325	Large-H
1000	312	Large-H	1000	326	Large-H

* NH - Non-hemolyzed
H - Hemolyzed

Weight Gain

A body weight loss and/or a reduced body weight gain were seen in at least one animal at all dose levels. The individual body weights are listed in Table 5.

TABLE 5 (Table Of Individual Body Weights (grams))

Dose (mg/kg)	Animal Number	Day 0	Day 7	Day 14 or (Terminal)
MALE RATS				
250	301	218	244	277
250	302	194	215	229
250	303	232	217	273
250	304	221	226	214
250	305	239	302	334
500	306	171	208	245
500	307	184	188	294
500	308	197	180	222
500	309	226	199	247
500	310	219	Died Day 1	*
1000	311	215	Died Day 2	(204)
1000	312	186	Died Day 2	(178)
1000	313	218	Died Day 1	*
1000	314	188	Died Day 1	*
1000	315	209	Died Day 1	*

* A terminal body weight was not recorded for any animal which died within 24 hours of dosing.

Table continued on next page.

TABLE 5, Continued (Table Of Individual Body Weights (grams))

Dose (mg/kg)	Animal Number	Day 0	Day 7	Day 14 or (Terminal)
FEMALE RATS				
250	316	162	187	208
250	317	169	186	206
250	318	155	177	188
250	319	152	168	152
250	320	163	Died Day 4	(141)
500	321	182	155	Died Day 10 (126)
500	322	177	197	196
500	323	162	186	205
500	324	157	116	Died Day 11 (99)
500	325	164	Died Day 2	(154)
1000	326	154	175	186
1000	327	158	Died Day 1	*
1000	328	165	Died Day 1	*
1000	329	171	Died Day 1	*
1000	330	167	Died Day 1	*

* A terminal body weight was not recorded for any animal which died within 24 hours of dosing.

Necropsy Findings

At necropsy, treatment-related changes seen in rats which died within 48 hours of dosing included blood in the stomach and intestinal tract, edema and red discoloration of the gastric mucosa, blood in the urinary bladder, dark and enlarged spleens, wet facial hair caused by salvia, and inguinal hair that was either stained by urine or discolored red by urine.

Treatment-related changes noted in rats which died during the second week of the study included small thymus, adhesions of the stomach to the adjoining organs, edema and red discoloration of the gastric mucosa, a thickened non-glandular gastric mucosa, necrosis of the non-glandular gastric mucosa, small spleens, atrophy of the abdominal adipose tissue, urine-stained inguinal hair, and facial hair covered with porphyrin discharge.

For rats that survived to termination of the observation period, treatment-related changes included adhesions of the stomach to the adjacent organs; adhesions of the liver to the diaphragm, black watery contents in the stomach and intestinal tract; necrosis of the glandular gastric mucosa, duodenum and jejunum; red discoloration, hyperkeratosis, and thickening of the gastric mucosa; atrophy of the abdominal adipose tissue; and dry porphyrin stain on the hair of the face.

Incidental findings consisted of thymus hemorrhage, small testes in a single rat at the 500 mg/kg dose level, and lungs that did not collapse when the thoracic cavity was opened during necropsy.

In the absence of significant gross organ lesions other than signs of gastrointestinal irritation, no tissue was collected for microscopic examination. A detailed record of the incidence and severity of all gross abnormalities is presented in computer-generated tables which are included in the Appendix.

DISCUSSION

An acute oral toxicity study was conducted with rats administered 250, 500, or 1000 mg/kg of the test substance by gavage. The test substance, a liquid, was administered as received. For male rats, mortality was 0% at the 250 mg/kg dose level, 20% at the 500 mg/kg dose level, and 100% at the 1000 mg/kg dose level. For female rats, mortality was 20% at the 250 mg/kg dose level, 60% at the 500 mg/kg dose level, and 80% at the 1000 mg/kg dose level. The acute LD_{50} for this test substance was calculated to be 616 mg/kg for male rats and 445 for female rats.

The major clinical signs of abnormality observed during the 15-day observation period included body weight loss or a reduced body weight gain, slight to moderate weakness, a reduced amount of feces, porphyrin staining of the hair of the face, inguinal hair wet with urine, dehydration, black diarrhea, black fecal staining of the inguinal hair, excessive salivation, blood in the urine, and either wetness or staining of the inguinal hair by urine. In addition clinical signs noted prior to death included prostration, severe weakness, convulsions, pallor, gasping, and a lack of feces.

Although the cause of death for rats that died after exposure to the test substance was not identified, the major treatment-related changes observed at necropsy provided evidence that the test substance was a gastrointestinal irritant. These changes included ptyalism; necrosis, thickening, and edema of the glandular mucosa; hyperkeratosis of the non-glandular mucosa; and necrosis of the duodenum and jejunum. Other related changes seen at necropsy included adhesions of the stomach to adjoining organs, probably caused by leakage of the gastric juices through the stomach wall, and the presence of blood in the lumen of the stomach and intestinal tract. In the absence of significant gross organ lesions other than signs of gastrointestinal irritation, no tissue was collected for microscopic examination.

CONCLUSION

Based on the oral LD_{50} calculated by combining the male and female mortality data (545 mg/kg), the test substance was classified as slightly toxic in rats according to the criteria set forth by Hodge and Sterner (1949) and harmful if swallowed as defined in the 18th Adaptation of the EC Classification, Packaging, and Labelling of Dangerous Substances Directive.

REFERENCES

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APPENDIX

Study No. 97-0204
EAN 108872

PATHOLOGY REPORT

Test Substance: Cyclopropylamine

INTRODUCTION

Male and female rats given 1000, 500, or 250 mg/kg of the test substance by gavage, as part of an acute oral toxicity study, were necropsied. Necropsy lesions are listed in computer-generated tables.

The cause of death for rats that died after exposure to the test substance was not identified; however, necrosis in the gastrointestinal tract may have contributed to the deaths.

RESULTS

GROSS PATHOLOGY:

Male Rats - 1000 mg/kg dose group: Treatment-related changes in three rats which died on Day 1 and two rats which died on Day 2 included blood in the stomach (5/5), duodenum (4/5), and jejunum (4/5); moderate to severe red discoloration of the glandular (5/5) and non-glandular gastric mucosa (5/5); and minor to moderate edema of the glandular (5/5) and non-glandular gastric mucosa (5/5). The urine in the urinary bladder contained blood (2/5). The spleens were enlarged (2/5) and darker than normal (3/5). The hair of the face was either wet by saliva (3/5) or was stained red (1/5). The inguinal hair was discolored red by urine (3/5). The carcasses of four rats showed minor or moderate autolysis.

An incidental finding consisted of minimal or minor thymus hemorrhage (5/5).

Male Rats - 500 mg/kg dose group: Treatment-related changes in Rat 310 that died on Day 1 included blood in the stomach, duodenum, and jejunum; severe red discoloration of the glandular gastric mucosa, minor red discoloration of the non-glandular gastric mucosa; moderate edema of the glandular gastric mucosa; blood in the urinary bladder; enlarged and dark spleen; the inguinal hair was discolored red by urine; and the hair of the face was wet by saliva.

An incidental finding consisted of a minor thymus hemorrhage.

Treatment-related changes in the remaining four rats that survived the observation period included adhesions of the stomach to the adjacent organs (4/4), minor thickening of the glandular gastric mucosa (1/4), moderate or severe thickening of the non-glandular gastric mucosa (3/4), minor red discoloration of the non-glandular gastric mucosa (2/4) and minor hyperkeratosis of the non-glandular gastric mucosa (1/4). In addition, the adipose tissue was severely atrophied (1/4)and the inguinal hair was wet by urine (1/4).

Incidental findings consisted of moderately smaller testes in Rat 307.

Male Rats - 250 mg/kg dose group: Treatment-related changes in Rat 304 that survived the observation period included adhesions of the stomach to the adjoining organs; black watery contents in the stomach, duodenum, jejunum, ileum, and cecum; minor hyperkeratosis of the non-glandular gastric mucosa; and moderate necrosis of the glandular gastric mucosa, duodenum and jejunum. In addition, the ileum, cecum, colon, heart, liver, kidneys, spleen, testes, and skeletal muscles showed moderate pallor. The spleen was small and the inguinal hair was covered with dry fecal stain.

Treatment-related changes in the remaining four rats that survived the observation period included adhesions of the stomach to the adjoining organs (3/4), adhesion of the liver to the diaphragm (1/4) and minimal to moderate hyperkeratosis of the non-glandular gastric mucosa (4/4).

Female Rats - 1000 mg/kg dose group: Treatment-related changes in four rats which died on Day 1 included blood in the stomach (4/4); moderate or severe red discoloration of the glandular gastric mucosa (4/4), moderate edema of the glandular gastric mucosa (4/4); minor or moderate red discoloration of the non-glandular gastric mucosa (4/4), minor or moderate edema of the non-glandular gastric mucosa (2/4); enlarged (1/4) and dark spleens (4/4); red urine stain on the inguinal hair (1/4), and wet facial hair by saliva (1/4). The carcasses of four rats showed minor autolysis.

An incidental finding consisted of thymus hemorrhage (4/4).

Treatment-related changes in Rat 326 that survived the observation period consisted of a moderate hyperkeratosis of the non-glandular gastric mucosa.

Female Rats - 500 mg/kg dose group: Treatment-related changes in Rats 325, 321, and 324 that died on Days 2, 10, and 11, respectively, moderately small thymus (1/3); adhesions of the stomach to the adjoining organs (1/3); blood in the stomach (1/3); minor red discoloration of the non-glandular gastric mucosa (2/3); minor edema of the non-glandular gastric mucosa (1/3); moderately thickened non-glandular gastric mucosa (1/3); and moderate necrosis of the non-glandular gastric mucosa (1/3). In addition, the duodenum (1/3), jejunum (1/3), and urine in the

urinary bladder (1/3) contained blood; the spleens were small (2/3); and abdominal adipose tissue was moderately or severely atrophied (2/3). The inguinal hair was covered with dry urine stain (3/3), and the hair of the face was covered with porphyrin discharge (2/3). The carcasses of all three rats showed minor or moderate autolysis.

Incidental findings included lungs that did not collapse when the thoracic cavity was opened during necropsy (2/3) and minor thymus hemorrhage (2/3).

Treatment-related changes in the remaining two rats that survived the observation period included adhesions of the stomach to the adjoining organs (2/2), moderate hyperkeratosis (1/2) and moderate thickening of the non-glandular gastric mucosa (1/2), and dry porphyrin stain on the hair of the face (1/2).

Female Rats - 250 mg/kg dose group: Treatment-related changes in Rat 320 which died on Day 4 included severe red discoloration and moderate edema of the glandular gastric mucosa, minor red discoloration of the non-glandular gastric mucosa, dry urine stain on the inguinal hair, and dry porphyrin discharge on the hair of the face. The carcass of this rat showed moderate autolysis.

Treatment-related changes in the remaining four rats which survived the observation period included adhesions of the stomach to the adjoining organs (3/4), minimal or moderate hyperkeratosis of the non-glandular gastric mucosa (3/4), and severe atrophy of the abdominal adipose tissue (1/4).

In the absence of significant gross organ lesions other than the obvious signs of gastrointestinal irritation, no tissue was collected for microscopic examination.

COMMENTS:

No concurrent control group was available for observation. Therefore, the conclusions in this study were based on the experience of the pathologist with control animals from other studies.

Gross lesions which may be associated with the treatment were found in the heart, thymus, stomach, duodenum, jejunum, ileum, cecum, colon, liver, kidneys, urinary bladder, spleen, abdominal adipose tissue, testes, skeletal muscles, and hair.

The heart, ileum, cecum, colon, liver, kidneys, spleen, testes and skeletal muscles of Rat 304 (250 mg/kg) were pale probably from blood loss into the intestines.

In Rat 321 (500 mg/kg) the thymus was moderately reduced in size and the abdominal adipose tissue was severely atrophied. Both lesions were probably secondary to loss of body weight (on Day 1 this animal weighed 182g, terminal body weight on Day 10 was 126g).

In Rat 307 (500 mg/kg) the testes were moderately reduced in size and the abdominal adipose tissue was severely atrophied, however this rat gained normal body weight (on Day 1 this animal weighed 184g, terminal body weight on Day 14 was 294g). The cause of abdominal adipose tissue atrophy without the body weight loss, was not determined. The testes were moderately reduced in size but firm suggesting that they were hypoplastic and not atrophic. Atrophic testes are smaller than normal and soft from loss of the seminiferous epithelium. Hypoplasia is a congenital defect and not a sign of toxicity.

The gastric lesions included adhesions to the adjoining organs; blood in lumen; and red discoloration, necrosis, thickening and edema of the mucosa. In addition, the non-glandular gastric mucosa was hyperkeratotic.

Adhesions of the stomach to the adjoining organs was observed in Rats 301, 302, 304, 305, 317, 318 and 319 from the 250 mg/kg dose group, and in Rats 306-309, 321, 322 and 323 from the 500 mg/kg dose group. Similar lesions occur from leakage of the stomach juices through the stomach wall.

The incidences of lesions in the gastric mucosa in low, mid or high-dose groups of minor to severe red discoloration were 2, 8 and 18, minor to severe thickening 0, 6, 0, minor or moderate edema 1, 4, 16, and moderate necrosis 1, 1, and 0. In addition the incidences of minimal to moderate hyperkeratosis of the non-glandular gastric mucosa were 8, 2, and 1 for low, mid, or high-dose groups, respectively. The incidences of blood in the gastric lumen were 1, 2, and 9 for low, mid, or high-dose groups, respectively.

All of the above mentioned gastric lesions were probably due to irritation by the test substance.

The intestinal tract of Rat 304 (250 mg/kg) showed moderate necrosis of the duodenum and jejunum, and blood in the lumen of the duodenum, jejunum, ileum, and cecum. All of the intestinal lesions were probably due to irritation by the test substance.

Adhesion of the liver to the diaphragm in Rat 305 (250 mg/kg) was probably secondary to leakage of the stomach juices into the abdominal cavity.

Although the source of blood in the urinary bladder of Rats 310 and 325 (500 mg/kg) and Rats 311 and 312 (1000 mg/kg) was not determined, it was present in the mid and high-dose group rats only, and could be related to treatment.

Minor reduction in the size of the spleen in Rat 304 (250 mg/kg) was probably secondary to blood loss.

The hair of the face that was wet by saliva (ptyalism) was observed in Rats 310 (500 mg/kg) and Rats 313, 314, 315, and 329 (1000 mg/kg). Ptyalism or hypersecretion of saliva is characterized by profuse driveling from the mouth. The most likely cause of ptyalism in this study was irritation of the upper gastrointestinal tract by the test substance

Minor dry porphyrin discharge or minor red discoloration of the facial hair were observed in 1, 3, and 1 rats from the low, mid. and high-dose group, respectively. Stress is the most probable cause for porphyrin formation. Porphyrin discharge is occasionally observed in normal, untreated control rats. The incidence of this change lacked a dose-response relationship, therefore, it was not considered treatment-related.

Thymic hemorrhage observed in 0, 3, and 9 rats from the low, mid, or high-dose group rats, respectively was considered an agonal lesion, although it may have also occurred as a result of dissection of the thymus during necropsy.

Minimal to moderate urinary or fecal staining of the inguinal hair was observed in 2, 5, and 4 rats from the low, mid, or high-dose group rats, respectively.

Enlarged and/or dark spleen was observed in animals that died before study termination. This change is considered an agonal phenomenon not related to treatment.

CONCLUSIONS

The test substance was a gastrointestinal irritant as evidenced by ptyalism; and necrosis, thickening, and edema of the glandular mucosa; hyperkeratosis of the non-glandular mucosa; and necrosis of the duodenum and jejunum.

7/25/97
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7/25/97
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07/24/97

SUMMARY GROSS PATHOLOGY INCIDENCE TABLE - MALE RATS

GROUP	250 MG/KG	500 MG/KG	1000 MG/KG
TRACHEA	5	5	5
LUNGS	5	5	5
THYMUS	5	5	5
HEMORRHAGE	0	1	5
HEART	5	5	5
PALLOR	1	0	0
ESOPHAGUS	5	5	5
STOMACH	5	5	5
ADHESION	4	4	0
STOMACH, NON-GLANDULAR			
HYPERKERATOSIS	5	1	0
DISCOLORATION,RED	0	3	5
THICKENED	0	3	0
EDEMA	0	0	5
STOMACH, GLANDULAR			
NECROSIS	1	0	0
DISCOLORATION,RED	0	1	5
EDEMA	0	1	5
THICKENED	0	1	0
STOMACH CONTENTS			
INCREASED	1	1	5
DUODENUM	5	5	5
NECROSIS	1	0	0
INTESTINAL CONTENTS			
INCREASED	1	1	4
JEJUNUM	5	5	5
NECROSIS	1	0	0
INTESTINAL CONTENTS			
INCREASED	1	1	4
ILEUM	5	5	5
PALLOR	1	0	0
INTESTINAL CONTENTS			
INCREASED	1	0	0
CECUM	5	5	5
PALLOR	1	0	0
INTESTINAL CONTENTS			
INCREASED	1	0	0
COLON	5	5	5
PALLOR	1	0	0
RECTUM	5	5	5
LIVER	5	5	5
PALLOR	1	0	0
ADHESION	1	0	0
KIDNEYS	5	5	5
PALLOR	1	0	0

NUMBERS REPRESENT NUMBER OF TISSUES EXAMINED, OR IN THE CASE OF ABNORMAL FINDINGS, THE NUMBER OF TISSUES WITH EACH ABNORMALITY

SUMMARY GROSS PATHOLOGY INCIDENCE TABLE - MALE RATS

GROUP	250 MG/KG	500 MG/KG	1000 MG/KG
URINARY BLADDER	5	5	5
URINE			
DISCOLORATION,RED	0	1	2
PITUITARY GLAND	5	5	5
ADRENALS	5	5	5
PANCREAS, NOS	5	5	5
THYROID GLANDS	5	5	5
PARATHYROID GLANDS	5	5	5
SPLEEN	5	5	5
PALLOR	1	0	0
SMALL	1	0	0
ENLARGED,NOS	0	1	2
COLOR-DARKER THAN NORMAL	0	1	3
MESENTERIC LYMPH NODES	5	5	5
BONE MARROW	5	5	5
BRAIN	5	5	5
EYES	5	5	5
SALIVARY GLANDS	5	5	5
ADIPOSE TISSUE	5	5	5
ATROPHY	0	1	0
SKIN, NOS	5	5	5
HAIR	5	5	5
HAIR OF INGUINAL REGION			
HAIRCOAT, DRY FECAL STAIN	1	0	0
HAIRCOAT, DRY URINE STAIN	0	1	3
HAIRCOAT, WET BY URINE	0	1	0
HAIR OF FACE			
HAIRCOAT, WET BY SALIVA	0	1	3
DISCOLORATION,RED	0	0	1
ACCESSORY SEX ORGANS (MALE)	5	5	5
EPIDIDYMIDES	5	5	5
TESTES	5	5	5
PALLOR	1	0	0
SMALL	0	1	0
BODY AS A WHOLE, NOS	0	0	4
AUTOLYSIS	0	0	4
SKELETAL MUSCLE	1	0	0
PALLOR	1	0	0

NUMBERS REPRESENT NUMBER OF TISSUES EXAMINED, OR IN THE CASE OF ABNORMAL FINDINGS, THE NUMBER OF TISSUES WITH EACH ABNORMALITY

INDIVIDUAL ANIMAL GROSS PATHOLOGY INCIDENCE TABLE - MALE RATS

	250 MG/KG				
ANIMAL #	301	302	303	304	305
DAYS ON TEST	15	15	15	15	15
TRACHEA	X	X	X	X	X
LUNGS	X	X	X	X	X
THYMUS	X	X	X	X	X
HEART	X	X	X		X
PALLOR				3	
ESOPHAGUS	X	X	X	X	X
*STOMACH					
ADHESION	P	P		P	P
STOMACH, NON-GLANDULAR					
HYPERKERATOSIS	2	3	1	2	3
STOMACH, GLANDULAR					
NECROSIS				3	
STOMACH CONTENTS					
INCREASED				3	
*DUODENUM	X	X	X		X
NECROSIS				3	
INTESTINAL CONTENTS					
INCREASED				3	
*JEJUNUM	X	X	X		X
NECROSIS				3	
INTESTINAL CONTENTS					
INCREASED				3	
*ILEUM	X	X	X		X
PALLOR				3	
INTESTINAL CONTENTS					
INCREASED				3	
*CECUM	X	X	X		X
PALLOR				3	
INTESTINAL CONTENTS					
INCREASED				3	
COLON	X	X	X		X
PALLOR				3	
RECTUM	X	X	X	X	X
*LIVER	X	X	X		
PALLOR				3	
ADHESION					P
KIDNEYS	X	X	X		X
PALLOR				2	
URINARY BLADDER	X	X	X	X	X

KEY:N-NORMAL AND TISSUE COLLECTED FOR HISTOPATHOLOGY,1-MINIMAL,2-MINOR,3-MODERATE,4-SEVERE
P-PRESENT,A-ABSENT,*-SEE COMMENT REPORT, X=NORMAL BUT NOT COLLECTED

INDIVIDUAL ANIMAL GROSS PATHOLOGY INCIDENCE TABLE - MALE RATS

	250 MG/KG				
ANIMAL #	301	302	303	304	305
DAYS ON TEST	15	15	15	15	15
PITUITARY GLAND	X	X	X	X	X
ADRENALS	X	X	X	X	X
PANCREAS, NOS	X	X	X	X	X
THYROID GLANDS	X	X	X	X	X
PARATHYROID GLANDS	X	X	X	X	X
SPLEEN	X	X	X		X
PALLOR				2	
SMALL				2	
MESENTERIC LYMPH NODES	X	X	X	X	X
BONE MARROW	X	X	X	X	X
BRAIN	X	X	X	X	X
EYES	X	X	X	X	X
SALIVARY GLANDS	X	X	X	X	X
ADIPOSE TISSUE	X	X	X	X	X
SKIN, NOS	X	X	X	X	X
HAIR	X	X	X		X
HAIR OF INGUINAL REGION					
HAIRCOAT, DRY FECAL STAIN				1	
ACCESSORY SEX ORGANS (MALE)	X	X	X	X	X
EPIDIDYMIDES	X	X	X	X	X
TESTES	X	X	X		X
PALLOR				2	
SKELETAL MUSCLE					
PALLOR				3	

KEY:N-NORMAL AND TISSUE COLLECTED FOR HISTOPATHOLOGY,1-MINIMAL,2-MINOR,3-MODERATE,4-SEVERE
P-PRESENT,A-ABSENT,*-SEE COMMENT REPORT, X=NORMAL BUT NOT COLLECTED

INDIVIDUAL ANIMAL GROSS PATHOLOGY INCIDENCE TABLE - MALE RATS

	500 MG/KG				
ANIMAL #	306	307	308	309	310
DAYS ON TEST	15	15	15	15	1
TRACHEA	X	X	X	X	X
LUNGS	X	X	X	X	X
THYMUS	X	X	X	X	
HEMORRHAGE					2
HEART	X	X	X	X	X
ESOPHAGUS	X	X	X	X	X
*STOMACH					
ADHESION	P	P	P	P	
STOMACH, GLANDULAR					
DISCOLORATION,RED					4
EDEMA					3
THICKENED		2			
STOMACH, NON-GLANDULAR					
DISCOLORATION,RED		2	2		2
HYPERKERATOSIS	2				
THICKENED		4	3	4	
STOMACH CONTENTS					
INCREASED					3
*DUODENUM	X	X	X	X	
INTESTINAL CONTENTS					
INCREASED					3
*JEJUNUM	X	X	X	X	
INTESTINAL CONTENTS					
INCREASED					3
ILEUM	X	X	X	X	X
CECUM	X	X	X	X	X
COLON	X	X	X	X	X
RECTUM	X	X	X	X	X
LIVER	X	X	X	X	X
KIDNEYS	X	X	X	X	X
*URINARY BLADDER	X	X	X	X	
URINE					
DISCOLORATION,RED					2
PITUITARY GLAND	X	X	X	X	X
ADRENALS	X	X	X	X	X
PANCREAS, NOS	X	X	X	X	X

KEY:N-NORMAL AND TISSUE COLLECTED FOR HISTOPATHOLOGY,1-MINIMAL,2-MINOR,3-MODERATE,4-SEVERE
P-PRESENT,A-ABSENT,*-SEE COMMENT REPORT, X=NORMAL BUT NOT COLLECTED

INDIVIDUAL ANIMAL GROSS PATHOLOGY INCIDENCE TABLE - MALE RATS

	500 MG/KG				
ANIMAL #	306	307	308	309	310
DAYS ON TEST	15	15	15	15	1
THYROID GLANDS	X	X	X	X	X
PARATHYROID GLANDS	X	X	X	X	X
SPLEEN	X	X	X	X	
ENLARGED,NOS					2
COLOR-DARKER THAN NORMAL					3
MESENTERIC LYMPH NODES	X	X	X	X	X
BONE MARROW	X	X	X	X	X
BRAIN	X	X	X	X	X
EYES	X	X	X	X	X
SALIVARY GLANDS	X	X	X	X	X
ADIPOSE TISSUE	X		X	X	X
ATROPHY		4			
SKIN, NOS	X	X	X	X	X
*HAIR	X		X	X	
HAIR OF INGUINAL REGION					
HAIRCOAT, DRY URINE STAIN					2
HAIRCOAT, WET BY URINE		3			
HAIR OF FACE					
HAIRCOAT, WET BY SALIVA					1
ACCESSORY SEX ORGANS (MALE)	X	X	X	X	X
EPIDIDYMIDES	X	X	X	X	X
TESTES	X		X	X	X
SMALL		3			

KEY:N-NORMAL AND TISSUE COLLECTED FOR HISTOPATHOLOGY,1-MINIMAL,2-MINOR,3-MODERATE,4-SEVERE
P-PRESENT,A-ABSENT,*-SEE COMMENT REPORT, X=NORMAL BUT NOT COLLECTED

INDIVIDUAL ANIMAL GROSS PATHOLOGY INCIDENCE TABLE - MALE RATS

	1000 MG/KG				
ANIMAL #	311	312	313	314	315
DAYS ON TEST	2	2	1	1	1
TRACHEA	X	X	X	X	X
LUNGS	X	X	X	X	X
THYMUS					
HEMORRHAGE	1	2	2	2	2
HEART	X	X	X	X	X
ESOPHAGUS	X	X	X	X	X
*STOMACH					
STOMACH, GLANDULAR					
DISCOLORATION,RED	3	3	3	4	4
EDEMA	2	3	3	3	2
STOMACH, NON-GLANDULAR					
DISCOLORATION,RED	3	3	3	3	3
EDEMA	2	2	3	3	2
STOMACH CONTENTS					
INCREASED	3	3	3	3	3
*DUODENUM					X
INTESTINAL CONTENTS					
INCREASED	3	3	3	3	
*JEJUNUM					X
INTESTINAL CONTENTS					
INCREASED	3	3	3	3	
ILEUM	X	X	X	X	X
CECUM	X	X	X	X	X
COLON	X	X	X	X	X
RECTUM	X	X	X	X	X
LIVER	X	X	X	X	X
KIDNEYS	X	X	X	X	X
*URINARY BLADDER			X	X	X
URINE					
DISCOLORATION,RED	2	2			
PITUITARY GLAND	X	X	X	X	X
ADRENALS	X	X	X	X	X
PANCREAS, NOS	X	X	X	X	X
THYROID GLANDS	X	X	X	X	X
PARATHYROID GLANDS	X	X	X	X	X

KEY:N-NORMAL AND TISSUE COLLECTED FOR HISTOPATHOLOGY,1-MINIMAL,2-MINOR,3-MODERATE,4-SEVERE
P-PRESENT,A-ABSENT,*-SEE COMMENT REPORT, X=NORMAL BUT NOT COLLECTED

INDIVIDUAL ANIMAL GROSS PATHOLOGY INCIDENCE TABLE - MALE RATS

	1000 MG/KG				
ANIMAL #	311	312	313	314	315
DAYS ON TEST	2	2	1	1	1
SPLEEN	X	X			
ENLARGED,NOS			2		2
COLOR-DARKER THAN NORMAL			3	2	3
MESENTERIC LYMPH NODES	X	X	X	X	X
BONE MARROW	X	X	X	X	X
BRAIN	X	X	X	X	X
EYES	X	X	X	X	X
SALIVARY GLANDS	X	X	X	X	X
ADIPOSE TISSUE	X	X	X	X	X
SKIN, NOS	X	X	X	X	X
*HAIR					
HAIR OF FACE					
HAIRCOAT, WET BY SALIVA			1	1	1
DISCOLORATION,RED	2				
HAIR OF INGUINAL REGION					
HAIRCOAT, DRY URINE STAIN	1	1			1
ACCESSORY SEX ORGANS (MALE)	X	X	X	X	X
EPIDIDYMIDES	X	X	X	X	X
TESTES	X	X	X	X	X
BODY AS A WHOLE, NOS					
AUTOLYSIS	3	3	2		2

KEY:N-NORMAL AND TISSUE COLLECTED FOR HISTOPATHOLOGY,1-MINIMAL,2-MINOR,3-MODERATE,4-SEVERE
P-PRESENT,A-ABSENT,*-SEE COMMENT REPORT, X=NORMAL BUT NOT COLLECTED

SUMMARY GROSS PATHOLOGY INCIDENCE TABLE - FEMALE RATS

GROUP	250 MG/KG	500 MG/KG	1000 MG/KG
TRACHEA	5	5	5
LUNGS	5	5	5
COLLAPSE INCOMPLETE ON THORACOTOMY	0	2	0
THYMUS	5	5	5
HEMORRHAGE	0	2	4
SMALL	0	1	0
HEART	5	5	5
ESOPHAGUS	5	5	5
STOMACH	5	5	5
ADHESION	3	3	0
STOMACH, GLANDULAR			
DISCOLORATION,RED	1	2	4
EDEMA	1	2	4
STOMACH, NON-GLANDULAR			
DISCOLORATION,RED	1	2	4
HYPERKERATOSIS	3	1	1
EDEMA	0	1	2
THICKENED	0	2	0
NECROSIS	0	1	0
STOMACH CONTENTS			
INCREASED	0	1	4
DUODENUM	5	5	5
INTESTINAL CONTENTS			
INCREASED	0	1	4
JEJUNUM	5	5	5
INTESTINAL CONTENTS			
INCREASED	0	1	2
ILEUM	5	5	5
CECUM	5	5	5
COLON	5	5	5
RECTUM	5	5	5
LIVER	5	5	5
KIDNEYS	5	5	5
URINARY BLADDER	5	5	5
URINE			
DISCOLORATION,RED	0	1	0
PITUITARY GLAND	5	5	5
ADRENALS	5	5	5
PANCREAS, NOS	5	5	5
THYROID GLANDS	5	5	5
PARATHYROID GLANDS	5	5	5

NUMBERS REPRESENT NUMBER OF TISSUES EXAMINED, OR IN THE CASE OF ABNORMAL FINDINGS, THE NUMBER OF TISSUES WITH EACH ABNORMALITY

SUMMARY GROSS PATHOLOGY INCIDENCE TABLE - FEMALE RATS

GROUP	250 MG/KG	500 MG/KG	1000 MG/KG
SPLEEN	5	5	5
SMALL	0	2	0
ENLARGED,NOS	0	0	1
COLOR-DARKER THAN NORMAL	0	0	4
MESENTERIC LYMPH NODES	5	5	5
BONE MARROW	5	5	5
BRAIN	5	5	5
EYES	5	5	5
SALIVARY GLANDS	5	5	5
ADIPOSE TISSUE	5	5	5
ATROPHY	1	2	0
SKIN, NOS	5	5	5
HAIR	5	5	5
HAIR OF INGUINAL REGION			
HAIRCOAT, DRY URINE STAIN	1	3	1
HAIR OF FACE			
DRIED PORPHYRIN DISCHARGE	1	3	0
HAIRCOAT, WET BY SALIVA	0	0	1
FALLOPIAN TUBES	5	5	5
VAGINA	5	5	5
UTERUS	5	5	5
OVARIES	5	5	5
CERVIX UTERI	5	5	5
BODY AS A WHOLE, NOS	1	3	4
AUTOLYSIS	1	3	4

NUMBERS REPRESENT NUMBER OF TISSUES EXAMINED, OR IN THE CASE OF ABNORMAL FINDINGS, THE NUMBER OF TISSUES WITH EACH ABNORMALITY

INDIVIDUAL ANIMAL GROSS PATHOLOGY INCIDENCE TABLE - FEMALE RATS

	250 MG/KG				
ANIMAL #	316	317	318	319	320
DAYS ON TEST	15	15	15	15	4
TRACHEA	X	X	X	X	X
LUNGS	X	X	X	X	X
THYMUS	X	X	X	X	X
HEART	X	X	X	X	X
ESOPHAGUS	X	X	X	X	X
*STOMACH	X				
ADHESION		P	P	P	
STOMACH, GLANDULAR					
DISCOLORATION,RED					4
EDEMA					3
STOMACH, NON-GLANDULAR					
DISCOLORATION,RED					2
HYPERKERATOSIS		3	1	3	
DUODENUM	X	X	X	X	X
JEJUNUM	X	X	X	X	X
ILEUM	X	X	X	X	X
CECUM	X	X	X	X	X
COLON	X	X	X	X	X
RECTUM	X	X	X	X	X
LIVER	X	X	X	X	X
KIDNEYS	X	X	X	X	X
URINARY BLADDER	X	X	X	X	X
PITUITARY GLAND	X	X	X	X	X
ADRENALS	X	X	X	X	X
PANCREAS, NOS	X	X	X	X	X
THYROID GLANDS	X	X	X	X	X
PARATHYROID GLANDS	X	X	X	X	X
SPLEEN	X	X	X	X	X
MESENTERIC LYMPH NODES	X	X	X	X	X
BONE MARROW	X	X	X	X	X
BRAIN	X	X	X	X	X

KEY:N-NORMAL AND TISSUE COLLECTED FOR HISTOPATHOLOGY,1-MINIMAL,2-MINOR,3-MODERATE,4-SEVERE
P-PRESENT,A-ABSENT,*-SEE COMMENT REPORT, X=NORMAL BUT NOT COLLECTED

INDIVIDUAL ANIMAL GROSS PATHOLOGY INCIDENCE TABLE - FEMALE RATS

	250 MG/KG				
ANIMAL #	316	317	318	319	320
DAYS ON TEST	15	15	15	15	4
EYES	X	X	X	X	X
SALIVARY GLANDS	X	X	X	X	X
ADIPOSE TISSUE	X	X	X		X
ATROPHY				4	
SKIN, NOS	X	X	X	X	X
HAIR	X	X	X	X	
HAIR OF INGUINAL REGION					
HAIRCOAT, DRY URINE STAIN					2
HAIR OF FACE					
DRIED PORPHYRIN DISCHARGE					2
FALLOPIAN TUBES	X	X	X	X	X
VAGINA	X	X	X	X	X
UTERUS	X	X	X	X	X
OVARIES	X	X	X	X	X
CERVIX UTERI	X	X	X	X	X
BODY AS A WHOLE, NOS					
AUTOLYSIS					3

KEY:N-NORMAL AND TISSUE COLLECTED FOR HISTOPATHOLOGY,1-MINIMAL,2-MINOR,3-MODERATE,4-SEVERE
P-PRESENT,A-ABSENT,*-SEE COMMENT REPORT, X=NORMAL BUT NOT COLLECTED

INDIVIDUAL ANIMAL GROSS PATHOLOGY INCIDENCE TABLE - FEMALE RATS

	500 MG/KG				
ANIMAL #	321	322	323	324	325
DAYS ON TEST	10	15	15	11	2
TRACHEA	X	X	X	X	X
LUNGS		X	X		X
COLLAPSE INCOMPLETE ON THORACOTOMY	P			P	
THYMUS		X	X		
HEMORRHAGE				2	2
SMALL	3				
HEART	X	X	X	X	X
ESOPHAGUS	X	X	X	X	X
*STOMACH					
ADHESION	P	P	P		
STOMACH, GLANDULAR					
DISCOLORATION,RED				3	3
EDEMA				3	3
STOMACH, NON-GLANDULAR					
DISCOLORATION,RED				2	2
EDEMA					2
THICKENED	3	3			
NECROSIS	3				
HYPERKERATOSIS			3		
STOMACH CONTENTS					
INCREASED					2
*DUODENUM	X	X	X	X	
INTESTINAL CONTENTS					
INCREASED					2
*JEJUNUM	X	X	X	X	
INTESTINAL CONTENTS					
INCREASED					2
ILEUM	X	X	X	X	X
CECUM	X	X	X	X	X
COLON	X	X	X	X	X
RECTUM	X	X	X	X	X
LIVER	X	X	X	X	X
KIDNEYS	X	X	X	X	X
*URINARY BLADDER	X	X	X	X	
URINE					
DISCOLORATION,RED					2
PITUITARY GLAND	X	X	X	X	X
ADRENALS	X	X	X	X	X

KEY:N-NORMAL AND TISSUE COLLECTED FOR HISTOPATHOLOGY,1-MINIMAL,2-MINOR,3-MODERATE,4-SEVERE
P-PRESENT,A-ABSENT,*-SEE COMMENT REPORT, X=NORMAL BUT NOT COLLECTED

INDIVIDUAL ANIMAL GROSS PATHOLOGY INCIDENCE TABLE - FEMALE RATS

	500 MG/KG				
ANIMAL #	321	322	323	324	325
DAYS ON TEST	10	15	15	11	2
PANCREAS, NOS	X	X	X	X	X
THYROID GLANDS	X	X	X	X	X
PARATHYROID GLANDS	X	X	X	X	X
SPLEEN		X	X		X
SMALL	3			2	
MESENTERIC LYMPH NODES	X	X	X	X	X
BONE MARROW	X	X	X	X	X
BRAIN	X	X	X	X	X
EYES	X	X	X	X	X
SALIVARY GLANDS	X	X	X	X	X
ADIPOSE TISSUE		X	X		X
ATROPHY	4			3	
SKIN, NOS	X	X	X	X	X
*HAIR			X		
HAIR OF INGUINAL REGION					
HAIRCOAT, DRY URINE STAIN	3			3	2
HAIR OF FACE					
DRIED PORPHYRIN DISCHARGE	2	2		2	
FALLOPIAN TUBES	X	X	X	X	X
VAGINA	X	X	X	X	X
UTERUS	X	X	X	X	X
OVARIES	X	X	X	X	X
CERVIX UTERI	X	X	X	X	X
BODY AS A WHOLE, NOS					
AUTOLYSIS	3			2	3

KEY:N-NORMAL AND TISSUE COLLECTED FOR HISTOPATHOLOGY,1-MINIMAL,2-MINOR,3-MODERATE,4-SEVERE
P-PRESENT,A-ABSENT,*-SEE COMMENT REPORT, X=NORMAL BUT NOT COLLECTED

INDIVIDUAL ANIMAL GROSS PATHOLOGY INCIDENCE TABLE - FEMALE RATS

	1000 MG/KG				
ANIMAL #	326	327	328	329	330
DAYS ON TEST	15	1	1	1	1
TRACHEA	X	X	X	X	X
LUNGS	X	X	X	X	X
THYMUS	X				
HEMORRHAGE		2	2	2	1
HEART	X	X	X	X	X
ESOPHAGUS	X	X	X	X	X
*STOMACH					
STOMACH, GLANDULAR					
DISCOLORATION,RED		3	4	4	4
EDEMA		3	3	3	3
STOMACH, NON-GLANDULAR					
DISCOLORATION,RED		3	2	2	2
EDEMA		2		3	
HYPERKERATOSIS	3				
STOMACH CONTENTS					
INCREASED		3	3	3	3
*DUODENUM	X				
INTESTINAL CONTENTS					
INCREASED		3	3	3	3
*JEJUNUM	X	X	X		
INTESTINAL CONTENTS					
INCREASED				3	3
ILEUM	X	X	X	X	X
CECUM	X	X	X	X	X
COLON	X	X	X	X	X
RECTUM	X	X	X	X	X
LIVER	X	X	X	X	X
KIDNEYS	X	X	X	X	X
URINARY BLADDER	X	X	X	X	X
PITUITARY GLAND	X	X	X	X	X
ADRENALS	X	X	X	X	X
PANCREAS, NOS	X	X	X	X	X
THYROID GLANDS	X	X	X	X	X
PARATHYROID GLANDS	X	X	X	X	X

KEY:N-NORMAL AND TISSUE COLLECTED FOR HISTOPATHOLOGY,1-MINIMAL,2-MINOR,3-MODERATE,4-SEVERE
P-PRESENT,A-ABSENT,*-SEE COMMENT REPORT, X=NORMAL BUT NOT COLLECTED

INDIVIDUAL ANIMAL GROSS PATHOLOGY INCIDENCE TABLE - FEMALE RATS

	1000 MG/KG				
ANIMAL #	326	327	328	329	330
DAYS ON TEST	15	1	1	1	1
SPLEEN	X				
ENLARGED,NOS		2			
COLOR-DARKER THAN NORMAL		3	2	2	2
MESENTERIC LYMPH NODES	X	X	X	X	X
BONE MARROW	X	X	X	X	X
BRAIN	X	X	X	X	X
EYES	X	X	X	X	X
SALIVARY GLANDS	X	X	X	X	X
ADIPOSE TISSUE	X	X	X	X	X
SKIN, NOS	X	X	X	X	X
*HAIR	X	X	X		X
HAIR OF INGUINAL REGION					
HAIRCOAT, DRY URINE STAIN				2	
HAIR OF FACE					
HAIRCOAT, WET BY SALIVA				1	
FALLOPIAN TUBES	X	X	X	X	X
VAGINA	X	X	X	X	X
UTERUS	X	X	X	X	X
OVARIES	X	X	X	X	X
CERVIX UTERI	X	X	X	X	X
BODY AS A WHOLE, NOS					
AUTOLYSIS		2	2	2	2

KEY:N-NORMAL AND TISSUE COLLECTED FOR HISTOPATHOLOGY,1-MINIMAL,2-MINOR,3-MODERATE,4-SEVERE
P-PRESENT,A-ABSENT,*-SEE COMMENT REPORT, X=NORMAL BUT NOT COLLECTED

GROSS PATHOLOGY COMMENT REPORT

DAY	DOSE LEVEL	ANIMAL #	COMMENT
21	500.000 MG/KG	310	THE INGUINAL HAIR HAD A RED URINE STAIN.
21	500.000 MG/KG	310	THE STOMACH CONTAINED BLOOD.
21	500.000 MG/KG	310	THE DUODENUM CONTAINED BLOOD.
21	500.000 MG/KG	310	THE JEJUNUM CONTAINED BLOOD.
21	1000.000 MG/KG	313	THE STOMACH CONTAINED BLOOD.
21	1000.000 MG/KG	313	THE DUODENUM CONTAINED BLOOD.
21	1000.000 MG/KG	313	THE JEJUNUM CONTAINED BLOOD.
21	1000.000 MG/KG	314	THE STOMACH CONTAINED BLOOD.
21	1000.000 MG/KG	314	THE DUODENUM CONTAINED BLOOD.
21	1000.000 MG/KG	314	THE JEJUNUM CONTAINED BLOOD.
21	1000.000 MG/KG	315	THE INGUINAL HAIR HAD A RED URINE STAIN.
21	1000.000 MG/KG	315	THE STOMACH CONTAINED BLOOD.
22	1000.000 MG/KG	327	THE STOMACH CONTAINED BLOOD.
22	1000.000 MG/KG	327	THE DUODENUM CONTAINED BLOOD.
22	1000.000 MG/KG	328	THE STOMACH CONTAINED BLOOD.
22	1000.000 MG/KG	328	THE DUODENUM CONTAINED BLOOD.
22	1000.000 MG/KG	329	THE INGUINAL HAIR HAD A RED URINE STAIN.
22	1000.000 MG/KG	329	THE STOMACH CONTAINED BLOOD.
22	1000.000 MG/KG	329	THE DUODENUM CONTAINED BLOOD.
22	1000.000 MG/KG	329	THE JEJUNUM CONTAINED BLOOD.
22	1000.000 MG/KG	330	THE STOMACH CONTAINED BLOOD.
22	1000.000 MG/KG	330	THE DUODENUM CONTAINED BLOOD.
22	1000.000 MG/KG	330	THE JEJUNUM CONTAINED BLOOD.
22	1000.000 MG/KG	311	THE INGUINAL HAIR HAD A RED URINE STAIN.
22	1000.000 MG/KG	311	THE STOMACH CONTAINED BLOOD.
22	1000.000 MG/KG	311	THE DUODENUM CONTAINED BLOOD.
22	1000.000 MG/KG	311	THE JEJUNUM CONTAINED BLOOD.
22	1000.000 MG/KG	311	THE URINARY BLADDER CONTAINED BLOOD.

GROSS PATHOLOGY COMMENT REPORT

DAY	DOSE LEVEL	ANIMAL #	COMMENT
22	1000.000 MG/KG	312	THE INGUINAL HAIR HAD A RED URINE.
22	1000.000 MG/KG	312	THE STOMACH CONTAINED BLOOD.
22	1000.000 MG/KG	312	THE DUODENUM CONTAINED BLOOD.
22	1000.000 MG/KG	312	THE JEJUNUM CONTAINED BLOOD.
22	1000.000 MG/KG	312	THE URINARY BLADDER CONTAINED BLOOD.
22	500.000 MG/KG	325	THE INGUINAL HAIR HAD A RED URINE STAIN.
22	500.000 MG/KG	325	THE STOMACH CONTAINED BLOOD.
22	500.000 MG/KG	325	THE DUODENUM CONTAINED BLOOD.
22	500.000 MG/KG	325	THE JEJUNUM CONTAINED BLOOD.
22	500.000 MG/KG	325	THE URINARY BLADDER CONTAINED BLOOD.
22	500.000 MG/KG	321	THE STOMACH ADHERED TO THE LIVER AND ABDOMINAL WALL.
22	250.000 MG/KG	301	THE STOMACH ADHERED TO THE LIVER AND ABDOMINAL WALL.
22	250.000 MG/KG	302	THE STOMACH ADHERED TO THE LIVER AND ABDOMINAL WALL.
22	250.000 MG/KG	304	THE STOMACH ADHERED TO THE LIVER AND ABDOMINAL WALL.
22	250.000 MG/KG	304	THE STOMACH CONTAINED BLACK WATERY CONTENTS.
22	250.000 MG/KG	304	THE DUODENUM CONTAINED BLACK WATERY CONTENTS.
22	250.000 MG/KG	304	THE JEJUNUM CONTAINED BLACK WATERY CONTENTS.
22	250.000 MG/KG	304	THE ILEUM CONTAINED BLACK WATERY CONTENTS.
22	250.000 MG/KG	304	THE CECUM CONTAINED BLACK WATERY CONTENTS.
22	250.000 MG/KG	305	THE STOMACH ADHERED TO THE LIVER AND DIAPHRAGM.
22	250.000 MG/KG	305	THE LIVER ADHERED TO THE DIAPHRAGM.
22	500.000 MG/KG	306	THE STOMACH ADHERED TO THE LIVER AND ABDOMINAL WALL.
22	500.000 MG/KG	307	THE STOMACH ADHERED TO THE LIVER, LEFT KIDNEY,SPLEEN, AND AB DOMINAL WALL.
22	500.000 MG/KG	309	THE STOMACH WAS ADHERED TO THE LIVER, SPLEEN, AND ABDOMINAL WALL.
22	250.000 MG/KG	317	THE STOMACH ADHERED TO THE LIVER AND SPLEEN.
22	250.000 MG/KG	318	THE STOMACH WAS ADHERED TO THE SPLEEN AND ABDOMINAL WALL.
22	250.000 MG/KG	319	THE STOMACH ADHERED TO THE SPLEEN.
22	500.000 MG/KG	322	THE STOMACH WAS ADHERED TO THE LIVER, SPLEEN AND ABDOMINAL W ALL.
22	500.000 MG/KG	323	THE STOMACH ADHERED TO THE LIVER AND SPLEEN.
29	500.000 MG/KG	310	THE URINARY BLADDER CONTAINED BLOOD.
30	500.000 MG/KG	308	THE STOMACH ADHERED TO THE LIVER, SPLEEN, AND ABDOMINAL WALL.